General

Guideline Title

The role of IMRT in head & neck cancer.

Bibliographic Source(s)

O'Sullivan B, Rumble RB, Warde P, IMRT Indications Expert Panel. The role of IMRT in head & neck cancer. Toronto (ON): Cancer Care Ontario (CCO); 2011 Jan 12. Various p. (Evidence-based series; no. 21-3-3). [69 references]

Guideline Status

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Recommendations

Major Recommendations

- If the reduction of xerostomia and improved quality of life are the main outcomes of interest, then intensity-modulated radiation therapy (IMRT) is the recommended treatment for all nasopharyngeal, oropharyngeal, hypopharyngeal, laryngeal, oral cavity, and unknown primary cancers where lymph node regions requiring inclusion in the treatment volume would result in irreparable damage to salivary function if two-dimensional external beam radiotherapy (2D EBRT) or three-dimensional external beam radiotherapy (3D EBRT) were used due to their inability to maintain salivary doses within their tolerance limits (<26 Gy mean dose). The data provided are applicable to locally advanced disease but are equally applicable to early-stage disease and rare sites (e.g., salivary gland tumours) requiring RT that would otherwise damage these normal structures. In addition, these principles hold for skin malignancy where advantages in sparing normal tissue while achieving target coverage are also relevant.
- If blindness is to be minimized or avoided, IMRT is indicated in the definitive or adjuvant RT setting for nasal and paranasal sinus cancers or other sites where the disease is juxtaposed to the optic apparatus. The latter would include diseases such as skin malignancy and sarcomas, in addition to epithelial cancers, since ocular toxicity is often a major barrier to safe treatment planning for lesions in these locations.
- If osteoradionecrosis is to be minimized or avoided, IMRT is indicated in the definitive or adjuvant RT of tumours in the oral cavity, oropharynx, paranasal sinuses, and nasopharynx where significant doses of RT are required and would be applied to the mandible if 2D EBRT or 3D EBRT were used.
- If treatment-related outcomes (local control, overall survival) are the main outcomes of interest, there are no randomized data to support or

refute a recommendation of IMRT over 2D EBRT or 3D EBRT in any head and neck site. However, nasopharyngeal cancer (NPC) should ordinarily be treated with IMRT based on treatment-related outcomes as should nasal and paranasal sinus cancer.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Head and/or neck cancer

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Oncology

Otolaryngology

Radiation Oncology

Intended Users

Allied Health Personnel

Other

Physicians

Utilization Management

Guideline Objective(s)

- To evaluate, in the treatment of nasopharyngeal cancer (NPC), if there is a benefit in local control, adverse effects, and quality of life measures associated with the use of intensity-modulated radiation therapy (IMRT) compared with two-dimensional external beam radiotherapy (2D EBRT)
- To evaluate, in the treatment of locally advanced head and neck (H&N) cancer, if there is a benefit in local control, adverse effects, and quality of life (QoL) measures associated with the use of IMRT compared with 2D EBRT

Target Population

Adult patients with head and/or neck cancer for whom treatment with radiation is being considered

Interventions and Practices Considered

1. Intensity-modulated radiation therapy (IMRT)
2. Two-dimensional external beam radiotherapy (2D EBRT)

Major Outcomes Considered

- Local control
- Overall survival
- Rates of xerostomia, osteoradionecrosis (specifically, mandible), optic nerve preservation, and dysphagia
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

The MEDLINE and EMBASE databases were searched for evidence on head & neck (H&N) cancer and intensity-modulated radiation therapy (IMRT) on March 20, 2009. In both databases, keywords for "head cancer" and "neck cancer" were combined with keywords for "intensity-modulated radiotherapy," and the following terms were excluded: "brachytherapy," "proton therapy," "biological markers," "gene therapy," "children," "childhood cancer," "pediatric cancer," "quality assurance," "treatment plan comparison," "aperture optimization," "independent dose calculation," "EPID dosimetry," and "set up errors." Results were limited to those published in English from the year 2000 to the current date in 2009. (See Appendix 2 in the original guideline document for the search results.)

A search for clinical practice guidelines (CPG), systematic reviews (SR), and health technology assessments (HTA) was also performed. A search of the National Guideline Clearinghouse (located at: http://www.guideline.gov) was performed on March 9, 2009. Additionally, a search of the MEDLINE and EMBASE databases was performed on March 25, 2009 using keywords for IMRT in combination with terms for all disease sites and limited to review articles published after 2000. The literature search strategies used for the MEDLINE and EMBASE databases appear in Appendix 2 in the original guideline document. Finally, the following were searched on March 25, 2009 using keywords for "IMRT", and "radiation" in combination with disease-site specific terms:

- Scottish Intercollegiate Guidelines Network (SIGN) (located at: http://www.sign.ac.uk)
- National Institute for Health and Care Excellence (NICE) (located at: http://www.nice.org.uk)
- Agency for Healthcare Research and Quality (AHRQ) (located at: http://www.ahrq.gov)

Conference proceedings of the annual meetings of the American Society of Radiation Oncology (ASTRO) and the American Society of Clinical Oncology (ASCO) were also searched from the year 2000 to current.

Study Selection Criteria

Inclusion Criteria

All of the following publication types must include comparative data on IMRT versus two-dimensional external beam radiotherapy (2D EBRT) and report on at least one of the outcomes of interest, including local control, osteoradionecrosis (specifically, mandible), xerostomia, optic nerve preservation, dysphagia, or quality of life (QoL).

- Clinical practice guidelines, systematic reviews, and health technology assessments
- Randomized phase II or phase III trials
- Dose escalation studies, toxicity reports, QoL reports, and retrospective studies

In addition, the publications:

- Must report on 50 or more patients
- Be published in English
- Be published in the year 2000 to current date

Exclusion Criteria

- Published in a language other than English
- Does not provide comparative data
- Reports on fewer than 50 patients
- Published prior to 2000

Number of Source Documents

Fifteen papers comprise the evidence in the systematic review, including four randomized controlled trial (RCT) reports on three RCTs, one prospective cohort study, eight retrospective cohort studies, one case-control study, and one cross-sectional study.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

No statistical analyses were planned in this systematic review but would be considered if data allow.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Evidence-Based Series (EBS) guidelines developed by Cancer Care Ontario's Program in Evidence-based Care (PEBC) use the methods of the Practice Guidelines Development Cycle. For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by one member of the IMRT Indications Expert Panel and one methodologist.

The systematic review is a convenient and up-to-date source of the best available evidence on the role of intensity-modulated radiation therapy (IMRT) in head and neck cancer. The body of evidence in this review is primarily comprised of published reports of comparative studies between IMRT and other methods of radiation delivery. That evidence forms the basis of the recommendations developed by the IMRT Indications Expert Panel. The systematic review and companion recommendations are intended to promote evidence-based practice in Ontario, Canada.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

IMRT Expert Panel Conference

On December 3, 2009, the intensity-modulated radiation therapy (IMRT) head & neck (H&N) cancers guideline was presented to the Expert Panel members (n=26), and feedback was obtained on the quality and comprehensiveness of the evidence and the recommendations.

Report Approval Panel

Following the presentation of this Evidence-based Series (EBS) draft report for Expert Panel review, the report was submitted on June 15, 2010 to the Program in Evidence-based Care (PEBC) Report Approval Panel (RAP) for review. The RAP is comprised of two members, including an oncologist, with expertise in clinical and methodological issues.

External Review: Professional Consultation

On September 20, 2010, the RAP-approved document was distributed to clinicians practicing within the Province of Ontario as part of a Profession Consultation review process. A total of 126 clinicians were invited to participate, and a total of 14 submitted responses (11% response rate) were received.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are supported by randomized controlled, cohort, case-controlled, and cross-sectional trials.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- One retrospective study with comparative data spanning five decades and a recent non-comparative report in paranasal sinus cancer suggest that blindness can be virtually eliminated, while treatment efficacy seems to be improved with intensity-modulated radiation therapy (IMRT) compared with two-dimensional external beam radiotherapy (2D EBRT). Despite the lower quality study design upon which this recommendation is based, this all-or-none outcome is considered clinically compelling and equivalent to what otherwise would be considered the highest and most compelling level of evidence.
- In the two randomized trials addressing nasopharyngeal cancer, locally advanced disease was not included, potentially based on the safety limitations associated with treating such tumours with non-IMRT techniques (as non-IMRT techniques are unable to avoid critical nearby structures). Single institution data and numerous similar reports from other institutions (not cited for purposes of brevity) and a multicentre phase II trial report by the Radiation Therapy Oncology Group (RTOG) consistently indicate that local control with IMRT exceeds 90% in nasopharynx cancer and significantly exceeds the control rates achieved by any group with non-IMRT techniques. One retrospective study with comparative data spanning five decades and a recent non-comparative study both report improved treatment efficacy with IMRT compared to other reports on patients not treated with IMRT in paranasal sinus cancers.

Potential Harms

Seven studies reported on some aspect of xerostomia, but only one retrospective cohort study reported on osteoradionecrosis and optic nerve preservation. None of the obtained studies reported on dysphagia. Of the seven studies reporting on xerostomia outcomes between intensity-modulated radiation therapy (IMRT) and two-dimensional radiation therapy (2D RT), five studies, totalling 400 patients, detected significant benefits in favour of IMRT. However, two of the studies obtained did not report any differences between IMRT and 2D RT for xerostomia. For osteoradionecrosis outcomes as reported in one study, only IMRT treatment was associated with no events, as both 2D RT and three-dimensional conformal radiation therapy (3D CRT) reported 5.5% and 3.9%, respectively. This same study also reported a significant benefit favouring treatment with IMRT compared with 2D RT or 3D CRT for optic nerve preservation (grade 3 or higher toxicity, IMRT: 0, 2D RT: 20%, 3D CRT: 9%; p=0.01). Table 6 in the original guideline document describes the adverse effects reported.

Qualifying Statements

Qualifying Statements

- The evidence obtained reported predominantly on reductions in late toxicities (specifically, xerostomia, blindness, and osteoradionecrosis of the mandible) that are also important in addressing quality of life (QoL). Treatment-related outcomes are not convincingly improved, but there is no indication that these outcomes are compromised as a result of intensity-modulated radiation therapy (IMRT). In general, the trend is toward an improvement in treatment-related outcomes. It should be noted that, in some situations, trials cannot be performed because of the inability to treat disease without danger to critical anatomy where damage could have catastrophic consequences. This is particularly applicable to the treatment of nasopharyngeal cancer (NPC) and paranasal sinus cancers.
- Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

O'Sullivan B, Rumble RB, Warde P, IMRT Indications Expert Panel. The role of IMRT in head & neck cancer. Toronto (ON): Cancer Care Ontario (CCO); 2011 Jan 12. Various p. (Evidence-based series; no. 21-3-3). [69 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Jan 12

Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

Guideline Developer Comment

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

Source(s) of Funding

The Program in Evidence-based Care (PEBC) and the Radiation Treatment Program (RTP) are supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC and any associated Programs is editorially independent from its funding source.

Guideline Committee

IMRT Indications Expert Panel and the Head & Neck Cancer Working Group

Composition of Group That Authored the Guideline

Steering Panel: Dr. Padraig Warde, Provincial Head, Radiation Treatment Program, Cancer Care Ontario; Mr. Eric Gutierrez, Program Manager, Radiation Treatment Program, Cancer Care Ontario; Ms. Kate Bak, Project Coordinator, Radiation Treatment Program, Cancer Care Ontario; Mr. Bryan Rumble, Research Coordinator, Program in Evidence-based Care, Cancer Care Ontario

Expert Panel: Dr. Anthony Whitton, Radiation Treatment Program, Cancer Care Ontario; Ms. Sarah Etheridge, Radiation Therapy Representative, Peel Regional Cancer Program; Ms. Lisa Favell, Capital Project Representative, Cancer Care Ontario; Ms. Katrina Fleming, Radiation Therapy Representative, Grand River Regional Cancer Centre; Ms. Esther Green, Chief Nursing Officer and Director of Health Human Resource Planning, Cancer Care Ontario; Dr. Konrad Leszczynski, Physics Representative, Northeastern Ontario Regional Cancer Centre; Dr. Michael Sharpe, Physics Representative, Princess Margaret Hospital

Working Group: Dr. Brian O'Sullivan, Radiation Oncologist, Head and Neck Cancer Program Leader, Princess Margaret Hospital, Professor, Department of Radiation Oncology, University of Toronto

Financial Disclosures/Conflicts of Interest

None declared

Guideline Status

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

Availability of Companion Documents

The following is available:

- Program in evidence-based care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2011. 15 p. Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on October 18, 2012.

Copyright Statement

Disclaimer

NGC Disclaimer

represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.